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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Massimo Bresciani

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EXAMINER

HELM, CARALYNNE E

ART UNIT

PAPER NUMBER

1615

NOTIFICATION DATE

DELIVERY MODE

10/05/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/506,715	Applicant(s) BRESCIANI ET AL.	
	Examiner CARALYNNE HELM	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 16-21 is/are pending in the application.
- 4a) Of the above claim(s) 16-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Note to Applicant: References to paragraphs in non-patent literature refer to full paragraphs (e.g. 'page 1 column 1 paragraph 1' refers to the first full paragraph on page 1 in column 1 of the reference).

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 25, 2010 has been entered.

Election/Restrictions

To summarize the election, applicant elected Group I with traverse.

Claims 16-21 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Harris et al. (US Patent No. 5,977,348).

Harris et al. disclose the crosslinking of starch by applying the crosslinking agent in densified carbon dioxide which is at supercritical conditions to starch (see column 12 lines 45-48 and column 20 lines 38-43). This crosslinked polymer is then treated with pure densified (supercritical) carbon dioxide under dynamic conditions (see column 12 lines 20-22, column 13 lines 28-31, and column 20 lines 38-43; instant claims 10 and 13-14). The preamble of instant claim 10, “to increase the drug-loading capacity of the cross-linked polymer” does not add any manipulative limitation to the claim (see MPEP 2105 II). Therefore the practicing of the recited method step by the prior art is sufficient to meet all of the claim limitations. Thus claims 10 and 13-14 are unpatentable over Harris et al.

Claims 10-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Koxholt et al. (US PGPub No. 2003/0049366).

Koxholt et al. disclose the application of a super critical carbon dioxide to crosslinked starch (see paragraph 44; instant claims 10 and 13-14). The exposure is done under both static and dynamic conditions (see table 1; instant claim 13). In addition, the exposure time is 90 minutes (see table 1; instant claims 11-12). The preamble of instant claim 10, "to increase the drug-loading capacity of the cross-linked polymer" does not add any manipulative limitation to the claim (see MPEP 2105 II). Therefore the practicing of the recited method step by the prior art is sufficient to meet all of the claim limitations. Thus claims 10-14 are unpatentable over Koxholt et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of *Graham v. John Deere Co.* have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lai et al. (previously cited) in view of Korsmeyer (Diffusion Controlled Systems: Hydrogels. Polymers for Controlled Drug Delivery. Ed. Peter J. Tarcha. Boca Raton: CRC Press, 1991 pg 20-22) and Carli et al. (previously cited).

Lai et al. teach a method where a cross-linked biodegradable polymer is treated with a pure supercritical fluid (see abstract and claim 12; instant claim 1). Specifically, Lai et al. teach that the cross-linked polymers can be polysaccharides, as well as ordinary synthetic polymers (see column 3 lines 38-48; instant claim 8). In a particular embodiment, the cross-linked polymer is taught to be treated with pure (free form any drug) supercritical carbon dioxide for 1 hour (see column 5 lines 18-21; instant claims 1-3 and 7). Although, Lai et al. teach that the supercritical fluid treated cross-linked

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polymers of their invention are useful as drug delivery systems, they do not teach the steps necessary to produce such a device (see column 4 lines 38-39).

Korsmeyer teaches a set of techniques known for loading drugs into polymer matrices (page 21 paragraph 5-page 22 paragraph 1). Within this limited listing includes the use of compressed (e.g., supercritical) carbon dioxide to swell the polymer and allow its impregnation with the drug (see page 22 paragraph 1).

Carli et al. teach a method of impregnating a cross-linked polymer with a drug (making a drug delivery system) using a supercritical fluid (see abstract; instant claim 1). Specifically, Carli et al. teach the steps where the drug is dissolved in the supercritical fluid, then the cross-linked polymer is contacted with this drug containing fluid impregnating the polymer with the drug, then the supercritical fluid is removed resulting in a drug loaded cross-linked polymer (see page 2 lines 6-10; instant claim 1).

Carli et al. go on to teach that the contacting of the drug loaded supercritical fluid can occur via a static and/or dynamic process for 15 minutes to 24 hours (see page 2 lines 22-26 and line 31-page 3 line 3; instant claims 4-6). The particular supercritical fluids taught for use in the process of Carli et al. include carbon dioxide, ethylene, propylene, and nitrous oxide (see page 2 lines 15-19; instant claim 7). Further, Carli et al. teach a collection of cross-linked polymers suitable for their process which include cross-linked polyvinyl pyrrolidone, cross-linked sodium carboxymethyl cellulose (interpreted as cross-linked cellulose), cross-linked sodium starch glycolate (interpreted as cross-linked starch), cross-linked polystyrene, and cross-linked acrylic acid, all of which fall into the categories of those taught by Lai et al. (see page 3 lines 17-22; instant claim 8).

Since 1) Korsmeyer teaches the loading of polymers with drug via swelling with compressed carbon dioxide as one of a small list of known options for drug loading methods and 2) Carli et al. teach the impregnation of crosslinked polymers with drug with supercritical carbon dioxide (a particular variety of compressed carbon dioxide), it would have been obvious to one of ordinary skill in the art at the time of the invention to select the method of Carli et al. to generate the drug delivery device suggested by Lai et al. as the application of a known technique to a similar device to yield the same result. This combination of references would result in the claimed method where a crosslinked polymer is treated (pre-treated) with a pure (free from any drug) supercritical fluid, then contacted with a supercritical fluid containing a dissolved drug, where the supercritical fluid is subsequently removed. Lai et al. in view of Korsmeyer and Carli et al. do not specifically teach that the drug precipitates inside the cross-linked polymer or the nature (amorphous character) of the drug. However, applicants' disclosure on page 2 of the specification states that the method of Carli et al. was employed by the applicant for the loading of drug via supercritical fluid (yielding precipitated drug in crosslinked polymer) and the desired characteristics (amorphous character) of the drug within the cross-linked polymer were attained (see instant specification page 2 lines 7-9 and 15-17). Thus the teachings of Lai et al. in view of Korsmeyer and Carli et al. meet the limitations of impregnated drug recited in instant claims 1 and 9. Therefore claims 1-9 are obvious over Lai et al. in view of Korsmeyer and Carli et al.

Claims 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lai et al. in view of Samain et al. (previously cited).

Lai et al. teach a method where a cross-linked biodegradable polymer is treated with a pure supercritical fluid after a crosslinking reaction is performed (see abstract and claim 12; instant claim 10). Specifically, Lai et al. teach that the cross-linked polymers can be polysaccharides, as well as ordinary synthetic polymers (see column 3 lines 38-48; instant claim 10). In a particular embodiment, the cross-linked polymer is taught to be treated with pure supercritical carbon dioxide for 1 hour (see column 5 lines 18-21; instant claims 11-14). Although, Lai et al. teach that the supercritical fluid treated cross-linked polymers of their invention are useful as drug delivery systems, Lai et al. do not teach starch or cellulose as particular polysaccharides.

Samain et al. teach biodegradable polymers envisioned for use in drug delivery (see column 1 lines 6-8). Samain et al. go on to teach cross-linked cellulose and cross-linked starch as particular biodegradable polymers of the invention (see column 2 lines 64-66; instant claim 10).

It would have been obvious to one of ordinary skill in the art to select starch or cellulose, as taught by Samain et al, for the particular polysaccharides used in the method of Lai et al. since they were taught for use in crosslinked form in drug delivery devices and Lai et al. teach the crosslinked polymer product of their method in drug delivery devices. The preamble of instant claim 10, "to increase the drug-loading capacity of the cross-linked polymer" does not add any manipulative limitation to the claim (see MPEP 2105 II). Therefore the practicing of the recited method step by the

prior art is sufficient to meet all of the claim limitations. Thus claims 10-14 are obvious over Lai et al. in view of Samain et al.

Response to Arguments

Applicants' arguments, filed February 25, 2010, have been fully considered.

Regarding rejection under 35 USC 103(a) over Lai et al. in view of Carli et al.:

Applicants' arguments concerning the motivation to combine the references as presented in the rejection is persuasive. Therefore the rejection has been modified to include a reference that supports the contention previously made that supercritical fluid loading was one of a small number of options known by the artisan of ordinary skill for loading drugs into a polymer matrix.

Although applicants further argue that the interpretation of the pure supercritical fluid treatment of a crosslinked polymer in Lai et al. as a "pre-treatment" is improper hindsight, the choice by applicants to title the application of pure super-critical fluid to a crosslinked polymer as a "pre-treatment" does not add any limitations to the application process. This treatment step in Lai et al. and the instant application is the same. While the phenomenon occurring in the polymer as a result of the treatment may be explained differently by Lai et al., the method is still the same as that instantly claimed.

Regarding presentation of unexpected results:

Applicants reiterate examples in the instant specification that were referenced as demonstrating unexpected results.

Upon further consideration, applicants' arguments that the teachings of Domingo et al. and Berens et al. do not dispute the results that applicants highlight as unexpected are persuasive. However, the highlighted unexpected results are not commensurate in scope with the claims as recited. Presently the claims do not require a particular degree of crystallinity in the in final product, a particular duration of exposure to the drug containing supercritical fluid, or a particular rate of drug loading that is aligned with the data highlighted in the specification. In addition, prior art demonstrates that the disbursement of a drug into a polymer with supercritical fluid such that the drug is completely non-crystalline is possible without the pre-treatment step instantly recited (see Karzarian et al. International Journal of Pharmaceutics January 2002 232:81-90 note page 86 column 1 paragraph 1-column 2 line 5). Therefore the discussion of unexpected results is not persuasive.

Regarding rejection under 35 USC 103(a) over Lai et al. in view of Samain et al.:

Applicants argue that the vector, as opposed to the polymer, taught in Samain et al. acts as the drug delivery device. They conclude that the teachings of Samain et al. were not considered in their entirety. Samain et al. explicitly teach a crosslinked polymer matrix that serves as the carrier for the vector (see column 4 lines 5-23). Moreover, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the

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claimed invention must be expressly suggested in any one or all of the references.

Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In this instance, the combined teachings of Lai et al. in view of Samain et al. render the instant claim obvious as detailed in the rejection.

Applicants further argue that one of ordinary skill in the art would not have looked to Samain et al. in effort to practice the instant invention. According to MPEP 2144 III, “[t]he reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See, e.g., *In re Kahn*, 441 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).” Thus the artisan of ordinary skill would not have to be motivated by the same goal as applicant in order to combine the cited references and render the claimed invention obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Juliet C Switzer/

Primary Examiner, Art Unit 1634